

The University of Chicago

I. THE EFFECT OF COBALTOUS CHLORIDE
ON THE REACTION OF METHYL-
MAGNESIUM BROMIDE WITH
ALICYCLIC CHLORIDES

II. THE NON-COPLANAR FREE
1-APOCAMPHYL RADICAL

A DISSERTATION SUBMITTED TO THE FACULTY
OF THE DIVISION OF THE PHYSICAL SCIENCES
IN CANDIDACY FOR THE DEGREE OF DOCTOR
OF PHILOSOPHY

DEPARTMENT OF CHEMISTRY
DECEMBER, 1943

By
FRANCES M. ENGELMANN

CHICAGO, ILLINOIS

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ACKNOWLEDGMENT

The author takes great pleasure in acknowledging her gratitude to Professor M. S. Kharasch for his invaluable advice and guidance during the course of this investigation.

PART I

THE EFFECT OF COBALTOUS CHLORIDE ON THE REACTION OF METHYLMAGNESIUM BROMIDE WITH ALICYCLIC CHLORIDES

INTRODUCTION

It has been shown¹ that, in the presence of cobaltous chloride, phenylmagnesium bromide reacts with aliphatic halides (methyl, ethyl, propyl, n-butyl bromides and t-butyl chloride) to yield biphenyl and the saturated and unsaturated hydrocarbon of the alkyl halides used. The formation of these hydrocarbon gases has been explained by assuming the intermediate formation of cobaltous subhalide (a chain carrier) which, by removing a halogen atom from the alkyl halide, forms the aliphatic free radicals which, in turn, either remove a hydrogen atom from the solvent or disproportionate to a mixture of equal quantities of the saturated and unsaturated hydrocarbons. Since little is known of the behavior of alicyclic free radicals in solution, it was desirable to make in this series quantitative studies similar to the one cited. Accordingly, the reactions of cyclohexyl chloride, the two 2-methylcyclohexyl chlorides, bornyl and isobornyl chlorides with methylmagnesium bromide in the presence and in the absence of cobaltous chloride were investigated.

DISCUSSION

Reaction of alicyclic chlorides with methylmagnesium bromide.—The results obtained by heating methylmagnesium bromide with various alicyclic chlorides for 28 hours are given in Table 1. These results are readily explained by assuming that the normal condensation reaction is extremely slow, and that, conse-

¹Kharasch, Lewis and Reynolds, J. Am. Chem. Soc., **63**, 493 (1943).

TABLE 1

REACTION OF METHYLMAGNESIUM BROMIDE WITH
ALICYCLIC CHLORIDES

Alicyclic Halide	% Reaction ^a	Addition Product	Unsaturated Compound	Gas Evolved
2-methyl cyclohexyl chloride (trans)	46	10	33	100% methane
2-methyl cyclohexyl chloride (cis)	49	10	34	100% methane
Bornyl chloride. .	5	..	..	
Isobornyl chloride	90	..	90	100% methane

^aThe extent of the reaction was determined by halogen titration. (Kharasch and Fields, J. Am. Chem. Soc., **63**, 2311 [1941].)

quently, the secondary reaction (elimination of hydrogen chloride and formation of the unsaturated compound) predominates. As would be expected, the gas formed in the reaction is pure methane. It is of considerable theoretical interest that, although the cis and trans forms of 2-methyl cyclohexyl chloride give the same reaction products, bornyl and isobornyl chlorides differ considerably in their stability. Bornyl chloride is surprisingly stable with respect to the elimination of hydrogen chloride.

Reaction of methyl magnesium bromide with alicyclic chlorides in the presence of cobaltous chloride.--The reaction of methylmagnesium bromide and the alicyclic halides takes an entirely different course when about 5 mole per cent of cobaltous chloride is first added to the Grignard reagent. The results are summarized in Table 2. These catalyzed reactions are very much faster than the uncatalyzed ones. The reaction probably comes to an end while the reaction mixtures are allowed to warm from +5° to room temperature; they are certainly complete before the end of the first hour during which the mixture is kept at the boiling point of ether.¹ This enhanced reactivity in the presence of cobaltous chloride is particularly striking in the case of bornyl chloride, which, in the absence of cobaltous chloride, reacts only to the extent of 5%, even if the reaction mixture is heated for 28 hours.

The results recorded in Table 2 are best explained by a

¹Kharasch and Fields, J. Am. Chem. Soc., **63**, 2316 (1941).

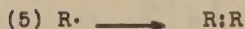
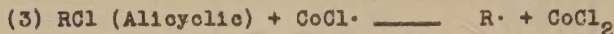
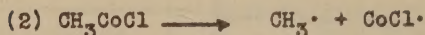
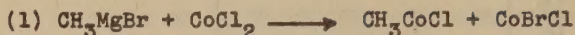
TABLE 2

REACTION OF METHYLMAGNESIUM BROMIDE WITH ALICYCLIC CHLORIDES IN THE PRESENCE OF COBALTOUS CHLORIDE^a

Alicyclic Halide	Reaction %	Dimer %	Unsaturated Compound %	Saturated Compound %	Gaseous Products		
					Methane %	Ethane %	Ethene %
Cyclohexyl chloride	86	26	29	27	85	9	6
2-methyl cyclohexyl chloride (trans)	87	27 ^b	23	28	77	15	8
2-methyl cyclohexyl chloride (cis)	89	22	31	34	83	9	8
Bornyl chloride	98	63	20	15	72	19	9
Isobornyl chloride	94	31	44	19	77	15	8

^aCobaltous chloride (5 mole per cent) was used in all experiments.^bAbout 6 per cent of an unidentified higher polymer was also isolated.

free radical chain reaction.



However, the alicyclic free radicals differ significantly from the lower aliphatic free radicals (up to butyl) in that reaction (5), the dimerization of the free radicals, does not occur with free aliphatic radicals, but takes place to the extent of 26% with the free cyclohexyl and 2-methyl cyclohexyl radicals, and to the extent of 63 % with the free bornyl radical. Since the free radicals derived from bornyl or isobornyl chloride are the same, the formation of 32 per cent less dimer from the isobornyl chloride can be ascribed only to the greater ease of elimination of hydrogen chloride from that molecule. The formation of equal quantities of the saturated and unsaturated hydrocarbons in the reaction with bornyl chloride, and the preponderance of the unsaturated over the saturated compound (44% to 19%) in the reaction with isobornyl chloride is in full agreement with this view.

The non-dimerization of the simple free alkyl radicals which do not possess sufficient energy to react with the solvent, and the dimerization of the free alicyclic, benzyl and substituted benzyl radicals, supports the hypothesis that only weakly electronegative radicals¹ have the tendency to dimerize. In this connection, it is important to note that, although resonance stability in the free radical is important in so far as the tendency to dimerize is concerned, the dimerization of free alicyclic radicals

¹For previous references see Kharasch, Reinmuth and Mayo, *J. Chem. Ed.*, **13**, 7 (1936); Kharasch and Kleiman, *J. Am. Chem. Soc.*, **65**, 491 (1943).

and other radicals in which resonance (as currently interpreted) plays only a minor part must have a different origin. The facts cited are compatible, however, with the view that only free radicals derived from weakly electronegative dimerize, and that the free benzyl or substituted benzyl radicals, which stabilize themselves through resonance, are members of a larger class of free radicals derived from weakly electronegative radicals, in many of which resonance plays only a very minor part. In other words, other things being equal, resonance is a sufficient but not a necessary condition for dimerization.

EXPERIMENTAL

Reagents.--Dow methyl bromide and Mallinckrodt magnesium turnings were used in the preparation of the Grignard reagent. The Grignard reagent was made by the method of Kharasch and Kleiman,¹ filtered through a sintered glass disc, and titrated for basicity and halogen immediately before being used.

Anhydrous cobaltous chloride was prepared by heating the hydrated salt at 150° in vacuo.

The bornyl chloride was prepared according to the directions of Fischer.² The pinene used was first distilled over sodium; the fraction boiling between 153° and 156° was used in the preparation.

Isobornyl chloride was prepared from camphene (m.p. 41.2-41.6) according to the directions of Meerwein and Van Emster.³ Cyclohexyl chloride and 2-methyl cyclohexyl chloride (cis) were prepared according to the directions of Zelinski.⁴ Trans-2-methyl cyclohexyl chloride was prepared according to the method given for menthyl chloride by Cumming, Hopper, and Wheeler.⁵

¹Kharasch and Kleiman, *ibid.*

²Fischer, "Laboratory Manual of Organic Chemistry," John Wiley and Sons, New York, 1920, p. 198.

³Meerwein and Van Emster, *Ber.*, **55**, 2526 (1922).

⁴Zelinski, *Ber.*, **41**, 2679 (1908).

⁵Cumming, Hopper and Wheeler, "Systematic Organic Chemistry," Constable, London, 1937, p. 335.

Procedure.--The Grignard reactions were carried out according to the directions of Kharasch, Lewis and Reynolds,¹ with two modifications: a trap cooled in dry ice was placed between the reaction flask and the gas collector, and a 10% excess of Grignard reagent was used. Twenty gram samples were used in the reactions with bornyl and isobornyl chlorides. With the 2-methyl cyclohexyl chlorides and cyclohexyl chloride, 50-gram samples were used in the cobaltous chloride catalyzed reactions, and 25-gram samples in the control experiments. In the reactions catalyzed by cobaltous chloride, the mixtures were refluxed for 5 hours and allowed to stand overnight. In the control experiments where no cobaltous chloride was used, refluxing was continued for 28 hours.

In all experiments, after the excess Grignard reagent was decomposed with dilute acetic acid, the aqueous solution was extracted three times with ether, and the extracts combined. The ether solution was then washed twice with water, once with 5% sodium carbonate solution, and twice more with water. All aqueous washings were combined and diluted to standard volume; an aliquot portion was titrated for halogen (Volhard method) to determine the extent of the reaction.

Analysis.--The reaction products from the bornyl and isobornyl chloride runs were analyzed by the method of Hesse.² The amount of dibornyl was determined by distilling the ether from an aliquot portion of the ether extracts. The residue was heated on a steam bath. A stream of air was blown over the warm material until the loss in weight per hour came to a small constant value. The weight of the remaining residue corrected for the known loss was taken as the weight of dibornyl. In the analysis for camphene ether from another aliquot portion was removed by fraction distillation through a 37 centimeter column filled with single-turn glass helices. The last of the ether was removed in vacuo while the residue was maintained at -18° . The camphene was converted to the ester according to the directions of Bertram and Walbaum.³ The ester and mixed terpenes were dissolved in ether; the solution

¹Kharasch, Lewis, and Reynolds, loc. cit.

²Hesse, Ber., 38, 1132 (1906).

³Bertram and Walbaum, J. Pr. Chem., 49, 8 (1894).

was washed with water and with sodium carbonate. The ether was removed as before; the saponification equivalent of the mixture was determined by the method of Shriner and Fuson.¹ The formation of the ester and the saponification were conducted in a closed flask to avoid loss of the highly volatile camphene and ester. Corrections, determined by blank runs, were made for hydrogen chloride removed from the bornyl and isobornyl chlorides during the saponification, and for losses due to the volatility of camphene. The amount of camphane was determined by difference.

Dibornyl and camphane were identified by their melting points ($88-90^{\circ}$ and 150° respectively). Camphene was identified by conversion to the p-nitrobenzoyl ester of isoborneol (long needles, m.p. 133°). The melting point of this material was not lowered by admixture with a known sample of isobornyl p-nitrobenzoate.

In the reaction with cyclohexyl chloride and the 2-methyl cyclohexyl chlorides, the products were separated by fractional distillation in a 12 plate concentric tube column.

The product of the reaction between cyclohexyl chloride and methylmagnesium bromide in the presence of cobaltous chloride was distilled and the three following fractions collected: (1) $81-84^{\circ}$, a mixture of cyclohexene and cyclohexane; (2) b.p. 83° at 110 mm., unreacted cyclohexyl chloride; and (3) b.p. 68° at 2 mm., dicyclohexyl. The product of the reaction between 2-methyl cyclohexyl chloride and methyl magnesium bromide in the presence of cobaltous chloride was distilled and the following three fractions collected: (1) b.p. 63.5 to 67.5° at 140 mm; b.p. $101-104^{\circ}$ at 760 mm. (a mixture of methyl cyclohexene and methyl cyclohexane); (2) b.p. $101-102^{\circ}$ at 133 mm. (unreacted 2-methyl cyclohexyl chloride); (3) b.p. $104-106^{\circ}$ at 3 mm.; b.p. 252° at 760 mm. (2,2'-dimethyl dicyclohexyl). The amounts of unsaturation in the cyclohexene-cyclohexane and methylcyclohexane-methylcyclohexane fractions were determined by bromide-bromate titration.²

The gas analyses were made according to the procedure of Kharasch, Lewis, and Reynolds.³ The gas collected was in all

¹Shriner and Fuson, "Systematic Identification of Organic Compounds," John Wiley and Sons, New York, 1941, p. 117.

²"Scott's Standard Methods of Analysis," N. H. Furman, Ed., II, D. Van Nostrand Co., New York, 1939, p. 2253.

³Kharasch, Lewis and Reynolds, loc. cit.

cases approximately 70% of the amount calculated from the amount of reaction determined by Volhard titration.

Tables 1 and 2 (theoretical part) summarize the results obtained. The column headed "unsaturated compound" refers to camphene and bornylene in runs made with bornyl or isobornyl chloride and to methyl cyclohexene or cyclohexene in the runs with 2-methyl cyclohexyl chloride or cyclohexyl chloride. The "unsaturated compound" resulting from the reactions of bornyl and isobornyl chlorides is believed to be a mixture of camphene and bornylene because a 10% increase in unsaturation was observed when esterification was carried out under more drastic conditions.¹ Control samples of camphene gave the same unsaturation value when either method of esterification was used. The column headed "saturated compound" refers to camphane in the bornyl and isobornyl chloride runs, and to methyl cyclohexane or cyclohexane, respectively, in the runs with 2-methyl cyclohexyl chloride or cyclohexyl chloride.

¹Bredt and Hibbing, J. Pr. Chem., 84, 783 (1911).

SUMMARY

1. The reactions of some alicyclic chlorides with methylmagnesium bromide in the presence and absence of cobaltous chloride have been studied.

2. The significance of the formation of the dimers in the presence of cobaltous chloride is discussed.

PART II

THE NON-COPLANAR FREE 1-APOCAMPHYL RADICAL

INTRODUCTION

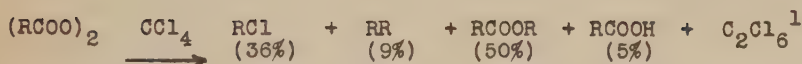
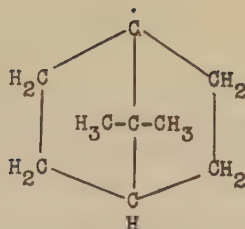
All free radicals hitherto described, whether of long half life period (expressed in years) or of short half life period (expressed in thousandth's of a second), assume a coplanar configuration. This coplanarity, presumably, accounts for the lack of optical activity of the reaction product, when a free radical produced from an optically active molecule reacts to form a molecule. Note, for instance, the optical inactivity of the 1,2-dichloro-2-methylbutane prepared by the chlorination of 1-chloro-2-methylbutane,¹ a reaction in which the free radical $(\text{CH}_3)(\text{C}_2\text{H}_5)\dot{\text{C}}\text{CH}_2\text{Cl}$ is an intermediate. It is, however, possible to prepare free radicals which cannot assume a coplanar configuration. Since the behavior of such free radicals in solution is of considerable theoretical interest, an investigation of a method for preparing one of these substances has been undertaken. The present work presents evidence for the existence of the non-coplanar free 1-apocamphyl radical.

DISCUSSION

Preparation and the reactions of the free 1-apocamphyl radical.--The free 1-apocamphyl radical was generated in carbon tetrachloride solution by heating the peroxide of apocamphane-1-carboxylic acid. The following products, in the quantities indicated, were isolated.

¹Kharasch and Brown, J. Am. Chem. Soc., **61**, 2142, 3432 (1939); **62**, 925 (1940); Brown, Kharasch, and Chao, J. Am. Chem. Soc., **62**, 3435 (1940).

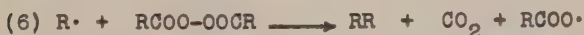
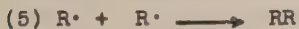
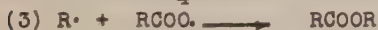
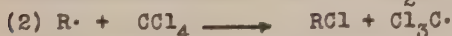
R = 1-apocamphyl radical =



The peroxide of apocamphane-1-carboxylic acid is unusually stable; it is completely decomposed only after being heated for about 20 hours in the carbon tetrachloride solution. The separation of the solvent and of the various reaction products was quite difficult. A vacuum technique had to be developed to separate the carbon tetrachloride from 1-chloroapocamphane and hexachloroethane, both of which are extremely volatile. These last two substances could not be separated by physical means, but it was found possible to destroy the hexachloroethane without breaking down the 1-chloroapocamphane, since the latter compound² is not readily attacked by inorganic bases. However, in spite of the difficulties mentioned, the course of the reaction was most satisfactory; no tar was formed, and it was possible to account quantitatively for all the peroxide used (see above).

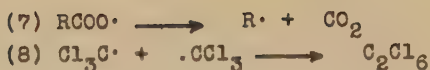
The formation of all the products found is probably best accounted for by the following mechanism.

R· = 1-apocamphyl radical



¹As expected, the molar yield of hexachloroethane was half of that of 1-chloroapocamphane.

²Bartlett and Knox, J. Am. Chem. Soc., **61**, 3184 (1939).



Formation of the ester and the dimer (bi-1-apocamphyl), according to reactions (4) and (6) seems more probable than their formation from the corresponding free radicals, as shown in reactions (3) and (5).¹

The type of decomposition given above is characteristic only for stable organic peroxides. Since the concentration of free radical resulting from the decomposition of such peroxides is at no time large, and since, in the experiments described, the yield of ester is about the same as the yield of chloro compound, the energy of activation required to remove a chlorine atom from carbon tetrachloride (reaction (2)) is probably about the same as that required to cleave the peroxide (reaction (3)).² Furthermore, the cleavage of the peroxide by the free 1-apocamphyl radical to yield the dimer (bi-1-apocamphane) (reaction (6)) requires a still higher energy of activation. The stability of the peroxide, its concentration, and the nature of the solvent thus determine the nature and the respective quantities of the reaction products. There is little doubt, however, that the free 1-apocamphyl radical is formed in solution and that this free radical is more reactive than the free trichloromethyl radical, since no products of the cleavage of the peroxide by this latter free radical have been noted.

EXPERIMENTAL

Preparation of the peroxide of apocamphane-1-carboxylic acid.--The peroxide of apocamphane-1-carboxylic acid was prepared by stirring a mixture of the acid chloride (3 g.), ether containing 5 drops of water (15cc), and sodium peroxide (.9g.) for 16

¹Another possible method of forming the ester RCOOR is by unimolecular decomposition of the peroxide into one molecule of carbon dioxide and one molecule of ester.

²Due allowance must of course be made for the fact that the solvent is at a higher concentration than the peroxide. The cleavage of the peroxide by the free 1-apocamphyl radical probably requires less activation energy than is required for the removal of a chlorine atom from a molecule of carbon tetrachloride.

hours at temperatures between -5° and 10° . The peroxide was taken up in ether, and the solution dried over anhydrous calcium chloride; the ether was then removed in a stream of dry air. The highly stable peroxide was crystallized from methyl alcohol. A sample of it was titrated¹ immediately before use; it proved to be 91% to 96% pure.

Decomposition of the peroxide of apocamphane-1-carboxylic acid in carbon tetrachloride.--The peroxide was dissolved in carbon tetrachloride (1:20) and the mixture refluxed for 20 hours. The reaction flask was connected through two traps (the first kept at 0° , the second at -80°) to a train consisting of two soda lime tubes, an Ascarite tube, a calcium chloride tube. This train led to a gas collector. No gas passed through the train into the gas collector during the reaction. After the reaction (when a test sample of the solution no longer oxidized potassium iodide), dry nitrogen was swept through the reaction flask and train for one hour. The increase in weight of the soda lime and Ascarite tubes was taken as the amount of carbon dioxide produced by the decomposition of the peroxide. This increase averaged 60% of the amount calculated for complete decomposition of the peroxide into carbon dioxide and organic radicals.

About three-fourths of the carbon tetrachloride was removed from the reaction product by fractional distillation through a 12 plate concentric tube column. The last of the carbon tetrachloride was removed from the volatile reaction products by fractional condensation on the vacuum line as follows. A small flask containing the concentrated mixture was connected to a fractionating system consisting of three U-tubes. The one nearest the flask was kept at 0° by ice; the second, at -27° by carbon tetrachloride mush; and the third, at -80° by dry ice. When the system was highly evacuated, the remaining carbon tetrachloride and some of the more volatile reaction product were distilled into the three U-tubes. Most of the distillate was fractionally condensed in the 0° and -27° tubes. This portion of the material was then distilled back into the flask by surrounding the flask with a -80° bath and heating the two U-tubes with steam. To remove the last traces of reaction product from the carbon tetrachloride solution

¹Kokatnur and Jelling, J. Am. Chem. Soc., 63, 1432 (1941).

trapped in the -80° U-tube, this portion of the material was distilled back and forth several times between the first and third U-tubes through the second tube held at -27° .

After all the carbon tetrachloride had been removed, the more volatile fraction of the residual reaction product was sublimed in vacuo. To remove the last traces of volatile material, the flask was heated on a steam bath, until the loss in weight per hour reached a small constant value. The weight of the residue was corrected for this small loss per hour due to sublimation of the less volatile products.

The volatile fraction proved to be composed wholly of hexachloroethane and 1-chloroapocamphane. The analysis of this mixture was simplified by the fact that the chlorine in 1-chloroapocamphane is not removed by the usual polar analytical reagents.¹ Accordingly, the hexachloroethane content of the mixture was determined by treating a sample with sodamide in liquid ammonia. The mixture was stirred over night and the residue was titrated for halogen by the Volhard method. Total halogen was determined in a Parr bomb. Using 0.1 N silver nitrate solution, a titre of 10.85 cc. for the halogen in the hexachloroethane and a titre of 14.44 cc. for the total halogen was calculated for 0.1 g. of the expected mixture of one mole of 1-chloroapocamphane with one-half mole of hexachloroethane. The values found were 10.68 and 13.63 cc., respectively.

1-chloroapocamphane was isolated from the mixture by decomposing the hexachloroethane with potassium hydroxide dissolved in diethylene glycol. The 1-chloroapocamphane was then removed by steam distillation. It was crystallized from dilute methyl alcohol and finally sublimed in high vacuo. It melted sharply at 170° to 171° . The melting point previously reported is $154-156^{\circ}$. However, the material here described was more carefully purified than the material obtained by Bartlett and Knox.

Anal. Calcd. for $C_9H_{15}Cl$: Cl, 22.4. Found: Cl, 22.1.

The non-volatile residue left after the steam distillation contained a small amount of material which was removed by hot 5%

¹Bartlett and Knox, J. Am. Chem. Soc., **61**, 3184 (1939).

sodium hydroxide solution. This material proved to be apocamphane-1-carboxylic acid; it was probably present as an impurity in the peroxide. The oil left after removal of the acid, was dissolved in ligroin and extracted four times with concentrated sulfuric acid. The ligroin solution was then washed with water, dried over anhydrous calcium chloride, and evaporated. The residue was the dimer, bi-1-apocamphyl (m.p. 216-217° [uncor.]).

Anal. Calcd. for $C_{18}H_{30}$: C, 88.74; H, 12.27. Found, C, 88.13; H, 12.10. Mol. wt. calcd. 246.4; found, 231.

The sulfuric acid extract was diluted with water. The organic material which separated was taken up in ligroin, and the ligroin evaporated. The residue was saponified with potassium hydroxide in diethylene glycol. This procedure yielded an acid and an alcohol. The acid was identified as apocamphane-1-carboxylic acid by its melting point (211°), its neutralization equivalent (167.2) and the fact that it did not lower the melting point of a known sample of apocamphane carboxylic acid. The alcohol was identified as 1-apocamphanol by its melting point 160-161° (uncor.). The ester extracted by the sulfuric acid was, therefore, 1-apocamphanyl apocamphane-1-carboxylate.

SUMMARY

1. The preparation of the peroxide of apocamphane-1-carboxylic acid is described.
2. The peroxide when heated in carbon tetrachloride solution gave the following reaction products: 1-chloroapocamphane, bi-1-apocamphyl, hexachloroethane, and 1-apocamphanyl apocamphane-1-carboxylate.
3. The mechanism of the decomposition is discussed.

